

Claims 24, 27 and 29 have been rejected under 35 U.S.C. §103 as obvious over German Offenlegungsschrift 2,064,474 and French Patent No. 1,093,728 considered together for reasons of record. Basically, the Examiner's position appears to be that the references taken together suggest the esters of the claimed compounds, and that, quoting the Examiner's first Office Action, "it is believed that the phosphoric acid compounds should be considered to be obvious over their corresponding esters." The Examiner has further indicated that the differences in phosphoric acid or ester group would not affect the properties of the claimed compounds since the anticonvulsant or anti-arrhythmic activity is due to the presence of the 5,5-diphenylhydantoin nucleus. Indeed, the Examiner has indicated that a prima facie case of obviousness exists, and that therefore actual and unexpected differences must be shown. Applicants strongly disagree with the Examiner's position.

To begin with, it is well-established in patent law that a chemical compound and all of its properties are inseparable. The thing patented is not the structural formula, but the compound itself. In re Papesch, 137 U.S.P.Q. 43. Accordingly, in order to determine obviousness, the question is whether the prior art, including structural formulas and description of properties, suggests to one of ordinary skill in the art to make the substitution or modification necessary to arrive at the claimed compound. If the prior art does not make such a suggestion, then no prima facie case of obviousness exists and the rejection under 35 U.S.C. §103 cannot be sustained.

Applying these general principles to the case at hand, we look first at the prior art of record, namely the cited French patent and OLS. Example 13 of French Patent No. 1,093,728 does indeed describe a single phosphoric acid ester whose acid is within the generic scope of present Claim 24, but not of Claims 27 and 29 which, by virtue of their dependency on Claims 25 and 27, respectively, are limited to compounds wherein X is O. Accordingly, the rejection of Claims 27 and 29 should be withdrawn on this basis alone. Offenlegungsschrift 2,064,474 appears to generically encompass the compound of Example 13 of the French patent as well as the corresponding esters having a  $(CH_2)_n$  bridge where n is 2 to 4, that is a  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$  or  $-CH_2CH_2CH_2CH_2-$  bridge. However, it is respectfully pointed out that the cited OLS does not disclose any phosphoric acid esters corresponding to the acids of present Claim 29. Thus, in addition to the difference in the value of X, when  $R_1$  is alkyl as in present Claim 29, the bridge between the nitrogen atom of the ring and X in the present compounds is a substituted methylene, i.e.,  $-CH-$  where  $R_1$  is  $C_1-C_7$  alkyl. Thus, in the presently claimed  $R_1$  compounds, a single carbon atom invariably separates N and X. Clearly then, the compounds of the OLS having ethylene or longer bridges are not esters of presently claimed acids and the 35 U.S.C. §103 rejection of Claim 29 should be withdrawn on this basis alone. Furthermore, it is pointed out that the OLS compounds having a  $CH_2$  bridge are esters of the very same acid whose ester is described in the French patent and thus are no more relevant than the compound of Example 13 of the French patent.

On the basis of structure alone, we thus see that the prior art describes phosphoric acid esters of a single acid encompassed by present Claim 24. The art of record contains absolutely no hint or suggestion of the formulas of the corresponding acids. Furthermore, as pointed out earlier, formulas are never to be considered alone in assessing obviousness. One must also consider what the prior art describes in the way of properties and what the prior art suggests as a whole to one of ordinary skill in the art. Returning then to the art of record, we find that the cited prior art teaches that its organophosphate esters are insecticides. THAT IS ALL THE ART OF RECORD TEACHES! The cited OLS and French patent contain absolutely no suggestion or hint of any kind that any of their esters would be useful for other than insecticidal purposes. Indeed, in view of the fact that organophosphate ester groupings are characteristic of an entire class of well-known insecticides which can vary considerably in the structure of the remainder of the molecule but which are always phosphate diesters or other disubstituted derivatives (e.g., tetraethylpyrophosphate, parathion, phosmet, phorate, paraoxon, crotoxyphos, naled and many others) and which are well-known to be cholinesterase inhibitors and thus extremely toxic to man as well as insects (causing acetylcholine poisoning, in which death may come from convulsions and respiratory paralysis), it is submitted that one of ordinary skill in the art would certainly not expect to use such organophosphate esters for the purposes of the present invention, i.e., as anti-convulsants, antiepileptics and anti-arrhythmics. Furthermore, it is submitted that to so pick and

choose only so much of the references (namely, the structure of the compounds) as will assist in supporting the Examiner's position to the exclusion of the other features (namely, insecticidal properties) necessary to the full appreciation of the teachings of those references is unwarranted and untenable, In re Wesslau, 147 U.S.P.Q. 391, and it totally out of keeping with the accepted principle that a compound and its properties are inseparable, In re Papesch, cited supra.

The Examiner has indicated that "it is not believed that the differences in phosphoric acid or ester group would effect the properties of the claimed compounds since the anti-convulsant or antiarrhythmic activity is due to the presence of 5,5-diphenyl-hydantoin nucleus." However, the Examiner has cited no prior art to substantiate this position. Applicants submit that, indeed, no generally recognized biological equivalency exists in the case of organophosphate esters and the corresponding acids. Most particularly, Applicants are unaware of any prior art teaching that acids of the type here claimed would be equivalent to the esters as insecticides (which is the only utility taught for the esters by the art of record), or of any prior art teaching that the esters could be used as anticonvulsants or antiarrhythmic agents (which would be most unusual in view of the general toxicity of organophosphate esters) or any prior art teaching that all 5,5-diphenylhydantoins, regardless of the identity of substituent groups, would be expected to have anticonvulsant or antiarrhythmic activity, or any prior art teaching that acids of the type here claimed would exhibit enhanced solubility and freedom from side effects as compared to diphenylhydantoin, as taught in

the present specification. If the Examiner is aware of such art, it is requested that it be cited so that Applicants can respond to it. In the absence of these additional citations, it is believed that the record 35 U.S.C. §103 rejection is not well-founded and that all of the claims of the present invention are clearly patentable over the art.

Claims 25 to 29 have been rejected under 35 U.S.C. §132 as being drawn to new matter and 35 U.S.C. §112, paragraph 1, the Examiner's position being that the claims encompass new subgeneric concepts which are not disclosed in the specification, and that the description of 3-phosphoryloxymethyl-diphenyl-hydantoin is not sufficient to support the new subgeneric groups encompassed by the claims. It is respectfully submitted that the Examiner's position is untenable and that the rejection should be withdrawn.

To begin with, the description must be considered as a whole in determining whether there is support for the claims and, when so considered, it is clear that the subject matter of Claims 25 to 29 is described in the specification and that said claims are therefore not drawn to new matter. Indeed, the Patent and Trademark Office has the initial burden of presenting evidence or reasons why those skilled in the art would not recognize in the specification a description of the invention defined by the claims, In re Wertheim, 191 U.S.P.Q. 90. It is respectfully submitted that the Examiner has not met that initial burden in the present case. And, in fact, it would be impossible for the Examiner to do so. The description of the compounds in the SUMMARY OF THE INVENTION in the instant specification is couched in Markush language, which is generally

understood to mean that Applicants are in fact asserting that, although the members of each Markush group do not fall within any recognized generic class, they are alternatively usable for the purposes of the invention, i.e., that, regardless of which values of R, R<sub>1</sub>, R<sub>2</sub>, X, etc., are substituted on the basic structure, the compound as a whole will exhibit the desired anticonvulsant, etc., activity. Thus, one skilled in the art would immediately recognize from the generic disclosure in the specification, the existence of the exact subclasses claimed in Claims 25 to 29. In other words, the exact subgenus claimed in each of Claims 25 to 29 is clearly discernable in the generalized formula in the specification and it is believed that In re Driscoll, 195 U.S.P.Q. 435, where the C.C.P.A. cautioned against hypertechnical application of the written description requirement, is directly in point.

In view of the fact that the language used in the SUMMARY OF THE INVENTION in the instant specification explicitly supports subgeneric Claims 25 to 29, it is not necessary to consider whether or not the compound 3-phosphoryloxymethyl-diphenylhydantoin implicitly or explicitly supports those claims. However, that compound alone certainly clearly supports at least Claims (25) and (27). oK

Claim 30 has been rejected under 35 U.S.C. §112, paragraph 2, as improperly depending on a cancelled claim and as not specifying the position of the two phenyl groups. By the amendment proposed hereinabove, the dependency of Claim 30 is corrected and the nomenclature is amended to reflect the location of the phenyl groups at the 5-position. Thus, all of the record rejections will be overcome with respect to Claim 30 by the amendments proposed hereinabove and it is

respectfully requested that these amendments, as well as the proposed correction of a typographical error in Claim 28, be entered.

In view of the foregoing, it is believed that all record rejections should be withdrawn. Further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

Respectfully submitted,

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